Changes induced by short-term xylene exposure in human evoked potentials

Anna Maria Seppäläinen*, Arto Laine, Tapani Salmi*, Vesa Riihimäki, and Elvi Verkkala

Institute of Occupational Health, Topeliuksenkatu 41a A, SF-00250 Helsinki, Finland

Summary. Nine healthy male volunteers were exposed to m-xylene for 3 h in the morning and 40 min in the afternoon with a 40-min break in between. The atmospheric m-xylene concentrations were either stable at 8.2 μmol/l (200 ppm) or they fluctuated (5.2–16.4 μmol/l; 135–400 ppm) with peaks of 16.4 μmol/l and duration of 20 min at the beginning of each exposure session. The subjects were either sedentary or exercised at 100 W for 10 min at the beginning of each session during both exposure types. The two control days, with and without exercise, were similar to the exposure days but without exposure. Evoked potentials were recorded in the morning before the exposure and immediately after the morning and afternoon sessions. Visual evoked potentials were studied to a pattern reversal stimulus (pattern VEP) and to a light flash (flash VEP). For pattern VEPs the latencies of P50, N70, P100, N135 and P170 as well as the peak-to-peak amplitude of N70 to P100 were measured. For flash VEPs the latencies of P50, N70, P100, N150 and P200 as well as the peak-to-peak amplitude of P100 to N150 were measured. Short-latency auditory evoked potentials arising in the brainstem (BAEP) were recorded for a click stimulus. The peaks I, II, III, IV and V were identified from the grand averages. The effect of various exposure paradigms was evaluated by comparing the individual changes on an exposure day to those during the control days. The latency N135 of the pattern VEP decreased in exposure at 400 ppm with exercise, and the latency P210 in the flash VEP decreased both at the stable and fluctuating exposure with exercise. The results might suggest some activation of the arousal level of the subjects after the most intensive exposure situations.

Key words: Xylene – Visual evoked potentials – Brainstem evoked potentials – Human experimental exposure

Introduction

Acute exposure to organic solvents may impair some functions of the central nervous system at concentrations which are much below the clearly narcotizing levels.

Experimental human studies have demonstrated changes in evoked potentials over short-term exposures to neurotoxic substances. Alterations in visual evoked potentials (VEP) have been reported after exposure to methylene chloride (1000 ppm) and trichloroethylene (100 ppm) for some hours (Stewart et al. 1972, 1974). Decrement in the amplitude of P200 component of the auditory evoked potential (AEP) has been reported after 3.5 h of exposure to trichloroethylene at 50 ppm (Winneke et al. 1978). Evoked potentials have been also utilized as a noninvasive and sensitive measure of the central nervous system function in studies on psychotropic drugs, in alcohol research, in anesthesiology as well as in the evaluation of long-term effects of industrial solvents (Obitz et al. 1977; Kalant 1978; Raitta et al. 1979; Seppäläinen et al. 1979; Elofsson et al. 1980; Genkina 1984; Cooper et al. 1985).

The present study was designed to show effects of varying m-xylene exposures in situations when the time-weighted average (TWA) concentration during different exposures was the same, namely 8.2 μmol/l. The effects on human evoked potentials were examined at stable or fluctuating exposures with higher exposures of short periods, both at rest and combined with exercise. The exposure conditions used are rele-

*Present address: Department of Neurology, University of Helsinki, Haartmaninkatu 4, SF-00290 Helsinki, Finland

Offprint requests to: A. M. Seppäläinen at her present address
vant to the actual exposures at workplaces, and were all within those limits allowed in work situations (TWA for 8 h 4.1 μmol/l in Finland).

Subjects and methods

Subjects. Nine male students volunteered for the study. Their mean age was 21 years, mean height 185 cm, mean weight 75 kg. Each subject was medically examined prior to the study. None of the subjects had a history of neurological, psychiatric or other chronic diseases, and the general physical as well as a detailed clinical neurological examination produced normal results. The results of the electroencephalography (EEG), chest X-ray, a cardiac function test (electrocardiography at rest and during submaximal ergometer exercise) and clinical chemical examinations were repeated after the exposure period, and no significant changes were noted.

None of the subjects used any drugs during the experimental period, and all of them were social consumers of alcohol. The use of alcohol was prohibited during the day and night before an experimental day. Blood alcohol concentration was analyzed in the morning of each experimental day and none was found in any of the subjects.

The study was approved by the ethics committee of the Institute of Occupational Health, Helsinki, and it was conducted with strict adherence to the ethical principles laid down by the World Medical Association (Declaration of Helsinki).

Exposures. The exposures to m-xylene (laboratory grade, Merck, FRG) were carried out in a dynamic exposure chamber in which the solvent concentration was continuously monitored and recorded (Riihimäki and Pfaffli 1978). A small amount of peppermint oil vapor was used on all exposure and control days to mask the presence or absence of the solvent.

Three groups of subjects with three persons in each were examined on six separate days. The only exception was one day when one subject was absent due to a cold. On two of the days each group was exposed to fixed 8.2 μmol/l (870 mg/m³ = 200 ppm) of m-xylene in the air. On the two other exposure days the basal concentration of m-xylene was 5.2 μmol/l (550 mg/m³ = 135 ppm) combined with a 20-min peak concentration of up to 16.4 μmol/l (1740 mg/m³ = 400 ppm) at the beginning of the morning and afternoon sessions. The subjects were either sedentary or exercised at 100 W for 10 min at the beginning of each session during both exposure types. Two control days, with and without exercise, were similar to the exposure days, but without exposure to xylene.

The subjects stayed in the chamber continuously for 3 h, and left the chamber for a 40-min break during which a standardized meal was served. After the break the subjects entered the chamber for an additional 40 min.

Venous blood samples were drawn during the experiments through a teflon catheter inserted into an antecubital vein. Venous blood concentrations of m-xylene were analyzed by gas chromatography (Riihimäki and Pfaffli 1978). The blood concentrations of m-xylene at a moment preceding by 5 to 7 min the time when the evoked potentials were measured are shown in Table 1.

The various exposure situations are as follows: 200 ppm R = exposure to a stable 200 ppm level of xylene in rest, 200 ppm E = exposure to a stable 200 ppm level of xylene with an exercise period of 10 min in the morning and at the beginning of the afternoon exposure, 400 ppm P + R = exposure to xylene with peak exposure periods of 400 ppm at rest, 400 ppm P + E = exposure to xylene with peak exposure periods of 400 ppm combined with exercise.

The experiments were conducted over consecutive weeks, and the control days preceded the exposure days in the same weeks so that the time interval since the former exposure to m-xylene was always at least 5 days. The experiments were single blind with a cross-over design, the subjects acting as their own controls. There are clear interindividual differences in the evoked potential measures, but using each subject as his own control this variation can be counteracted.

Electrophysiological methods. All the evoked potential recordings were taken three times on every experimental day, namely in the morning before the subjects entered the exposure chamber, at 12 noon right after the subjects left the exposure for a lunch break, and the last recording was made right after the cessation of a day's exposure. Three to five minutes elapsed between the end of exposure and the recordings, since the subjects had to come from the exposure chamber to the EEG laboratory on another floor. In each case the interval between the end of exposure and the recording was similar, since the subjects entered and left the exposure chamber in each exposure session at 20-min intervals.

Visual evoked potentials (VEP) were recorded from silver-silver chloride electrodes glued on mid-occipital (Oz) and mid-frontal (Fz) areas of the international 10-20 electrode placement system. The signals were amplified with a van Gogh electroencephalograph and then fed into a PDP 11 computer, where 60 responses were averaged on line. Both eyes were stimulated simultaneously first with a Grass pattern reversal stimulator (pattern VEP), and then with a light flash (flash VEP). The averaged responses were stored in the mass memory of the computer for later analysis. A joy stick operated pointer was set on various peaks on the computer screen, and the actual latencies and amplitudes were then measured by the computer program. For pattern VEPs the latencies of P50, N70, P100, N135 and P170 as well as the peak-to-peak amplitude of N70 to P100 were chosen for the analysis. For flash VEPs the latencies of P50, N70, P100, N150 and P200 as well as the peak-to-peak amplitude of P100 to N150 were chosen for the analysis.

Table 1 Blood m-xylene levels during different models. The venous solvent concentrations are given at the end of morning (180 min) and afternoon (260 min) sessions. The mean values and standard deviations are given

<table>
<thead>
<tr>
<th>Time of exposure</th>
<th>Stable 8.2 μmol/l of m-xylene</th>
<th>Exposure with peaks from 5.2 to 16.4 μmol/l of m-xylene</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood concentration (μmol/l)</td>
<td>At rest</td>
<td>During exercise</td>
</tr>
<tr>
<td>180 (min)</td>
<td>31.0 ± 6.8</td>
<td>28.2 ± 7.2</td>
</tr>
<tr>
<td>260 (min)</td>
<td>23.9 ± 6.0</td>
<td>29.9 ± 5.6</td>
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</tbody>
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